

IN THE CLAIMS:

Please cancel claims 1-8, 10-18, 20, 21, 23-27, 29, 30, 32, 44, 46 and 51-54; amend claims 33, 35, 37, 38, and 47; and add new claims 55-57 as follows:

33. (Twice Amended) An *in vitro* assay for a biological effect of presence of a protein or polypeptide or other product of DNA expression in a mouse embryonic stem (ES) cell, a mouse embryonal carcinoma (EC) cell or a mouse embryonic gonadal (EG) cell, or a differentiated derivative thereof, comprising the steps:

- (a) transfecting the mouse cell with a first episomal vector that expresses a viral replication factor;
- (b) transfecting the mouse cell of step (a) with a second vector, wherein
  - (i) the second vector contains a DNA coding for the protein or polypeptide or other product of DNA expression in operative combination with a promoter for expression of the DNA;
  - (ii) the second vector also contains a DNA coding for a selectable marker in operative combination with a promoter for expression of the selectable marker; and
  - (iii) the viral replication factor of step (a) replicates the second vector episomally;
- (c) isolating mouse cells of step (b); and
- (d) maintaining the isolated mouse cells over a plurality of generations so as to assay the biological effect of expression of the protein or polypeptide or other product of DNA expression.

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35. (Three Times Amended) The assay according to Claim 33, for assay of a biological effect of simultaneous presence of a first protein, polypeptide or other product of DNA expression and a second protein, polypeptide or other product of DNA expression in a mouse ES cell, a mouse EC cell or a mouse EG cell, or a differentiated derivative thereof, further comprising the step of transfecting the mouse cell of step (b) with a third vector, wherein the third vector contains

- (1) a DNA coding for the second protein, polypeptide or other product of DNA expression in operative combination with a promoter for expression of the DNA, and
- (2) a DNA coding for a selectable marker in operative combination with a promoter for expression of the selectable marker, wherein the viral replication factor of step (a) replicates the third vector episomally.

37. (Three Times Amended) An *in vitro* method of assaying whether a DNA under investigation codes for a polypeptide that directs transport of a cell active protein to a cell surface comprising the steps of:

- (a) expressing a composite DNA including (a) a DNA sequence under investigation, operatively linked to (b) a DNA coding for the cell active protein in a mouse cell, selected from the group consisting of an ES cell, an EC cell, an EG cell, and differentiated progeny thereof; wherein
  - (i) activity of the cell active protein is dependent upon transport of the cell active protein to the cell surface,
  - (ii) the DNA of (b) does not code for a polypeptide that directs transport of the cell active protein to the cell surface, and

(iii) the cell active protein inhibits differentiation of the cell and in the absence of the cell active protein the cell will differentiate; and

(b) determining if the cell differentiates.

38. (Twice Amended) The method according to Claim 37 wherein the DNA under investigation is a library of DNAs, which is screened to identify DNA sequences coding for signal polypeptide sequences that transport proteins to the cell surface, and wherein the method comprises the additional step of determining whether the cell active protein is transported to the cell surface and remains there or is secreted by the cell.

47. (Three Times Amended) The method according to Claim 37, wherein the composite DNA is expressed by:

- (a) (i) transfected the mouse cell with a first vector that expresses a viral replication factor; or
- (ii) otherwise obtaining a transgenic mouse cell, selected from the group consisting of an ES cell, an EC cell and an EG cell, that expresses the replication factor;
- (b) transfected the mouse cell of step (a) with a second vector, wherein
- (i) the second vector contains the composite DNA in operative combination with a promoter for expression of the composite DNA;
- (ii) the second vector also contains a DNA coding for a selectable marker in operative combination with a promoter for expression of the selectable marker; and

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- (iii) the viral replication factor of step (a) replicates the second vector episomally;
- (c) isolating mouse cells of step (b); and
- (d) maintaining the isolated mouse cells over a plurality of generations so as to assay the effect of expression of the composite DNA.
55. (New) The assay according to Claim 33, wherein the viral replication factor is a viral replication factor selected from polyoma large T antigen, EBNA-1 antigen, papilloma virus replication factors, and SV40 large T antigen.
56. (New) The assay according to Claim 33, wherein said second vector contains a DNA that codes for an anti-sense RNA.
57. (New) The assay according to Claim 33, further comprising the step: (e) isolating said DNA coding for the protein or polypeptide or other product of DNA expression.
58. (New) An *in vitro* assay for a biological effect of presence of first and second products of DNA expression in mouse embryonic stem (ES) cells, mouse embryonal carcinoma (EC) cells or mouse embryonic gonadal (EG) cells, comprising the steps:
- (a) transfecting the mouse cells with a first vector that expresses a viral replication factor;
- (b) isolating cells of step (a) and dividing the cells into at least a first sub-population of transfected cells and a second sub-population of transfected cells;
- (c) transfecting the first sub-population of transfected cells with a second vector, wherein the second vector contains a DNA coding for a first
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product of DNA expression in operative combination with a promoter for expression of the DNA and also contains a DNA coding for a selectable marker in operative combination with a promoter for expression of the selectable marker, and wherein the viral replication factor of step (a) replicates the second vector episomally;

- (d) isolating cells of step (c);
- (e) maintaining the isolated cells of step (d) over a plurality of generations so as to assay the biological effect of expression of the first product of DNA expression;
- (f) transfecting the second sub-population of transfected cells with a third vector, wherein the third vector contains a DNA coding for a second product of DNA expression in operative combination with a promoter for expression of the DNA and also contains a DNA coding for a selectable marker in operative combination with a promoter for expression of the selectable marker, and wherein the viral replication factor of step (a) replicates the third vector episomally;
- (g) isolating cells of step (f); and
- (h) maintaining the isolated cells of step (g) over a plurality of generations so as to assay the biological effect of expression of the second product of DNA expression.

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